

GAGCTCGGAT CCACTACTCG ACCACGCGT CCGGCCAGGA CCTCTGTGAA CCGGTCGGGG	60
CGGGGGCCGC CTGGCCGGGA GTCTGCTCGG CGGTGGGTGG CCGAGGAAGG GAGAGAACGA	120
TCGCGGAGCA GGGCGCCCGA ACTCCGGGCG CCGCGCC ATG CGC CGG GCC AGC CGA	175
Met Arg Arg Ala Ser Arg	
1 5	
GAC TAC GGC AAG TAC CTG CGC AGC TCG GAG GAG ATG GGC AGC GGC CCC	223
Asp Tyr Gly Lys Tyr Leu Arg Ser Ser Glu Glu Met Gly Ser Gly Pro	
10 15 20	
GGC GTC CCA CAC GAG GGT CCG CTG CAC CCC GCG CCT TCT GCA CCG GCT	271
Gly Val Pro His Glu Gly Pro Leu His Pro Ala Pro Ser Ala Pro Ala	
25 30 35	
CCG GCG CCG CCA CCC GCC GCC TCC CGC TCC ATG TTC CTG GCC CTC CTG	319
Pro Ala Pro Pro Pro Ala Ala Ser Arg Ser Met Phe Leu Ala Leu Leu	
40 45 50	

FIG.1A

GGG CTG GGA CTG GGC CAG GTG GTC TGC AGC ATC GCT CTG TTC CTG TAC	367
Gly Leu Gly Leu Gly Gln Val Val Cys Ser Ile Ala Leu Phe Leu Tyr	
55	60
	65
	70
TTT CGA GCG CAG ATG GAT CCT AAC AGA ATA TCA GAA GAC AGC ACT CAC	415
Phe Arg Ala Gln Met Asp Pro Asn Arg Ile Ser Glu Asp Ser Thr His	
75	80
	85
TGC TTT TAT AGA ATC CTG AGA CTC CAT GAA AAC GCA GGT TTG CAG GAC	463
Cys Phe Tyr Arg Ile Leu Arg Leu His Glu Asn Ala Gly Leu Gln Asp	
90	95
	100
TCG ACT CTG GAG AGT GAA GAC ACA CTA CCT GAC TCC TGC AGG AGG ATG	511
Ser Thr Leu Glu Ser Glu Asp Thr Leu Pro Asp Ser Cys Arg Arg Met	
105	110
	115
AAA CAA GCC TTT CAG GCG GCC GTG CAG AAG GAA CTG CAA CAC ATT GTG	559
Lys Gln Ala Phe Gln Gly Ala Val Gln Lys Glu Leu Gln His Ile Val	
120	125
	130

FIG.1B

GGG CCA CAG CGC TTC TCA GGA GCT CCA GCT ATG ATG GAA GGC TCA TGG	607
Gly Pro Gln Arg Phe Ser Gly Ala Pro Ala Met Met Glu Gly Ser Trp	
135 140 145 150	
TTG GAT GTG GCC CAG CGA GGC AAG CCT GAG GCC CAG CCA TTT GCA CAC	655
Leu Asp Val Ala Gln Arg Gly Lys Pro Glu Ala Gln Pro Phe Ala His	
155 160 165	
CTC ACC ATC AAT GCT GCC AGC ATC CCA TCG GGT TCC CAT AAA GTC ACT	703
Leu Thr Ile Asn Ala Ala Ser Ile Pro Ser Gly Ser His Lys Val Thr	
170 175 180	
CTG TCC TCT TGG TAC CAC GAT CGA GGC TGG GCC AAG ATC TCT AAC ATG	751
Leu Ser Ser Trp Tyr His Asp Arg Gly Trp Ala Lys Ile Ser <u>Asn</u> Met	
185 190 195	

FIG.1C

ACG TTA AGC AAC GGA AAA CTA AGG GTT AAC GAT GGC TTC TAT TAC	799
Thr Leu Ser Asn Gly Lys Leu Arg Val Asn Gln Asp Gly Phe Tyr Tyr	
200	210
205	
CTG TAC GCC AAC ATT TGC TTT CGG CAT CAT GAA ACA TCG GGA AGC GTA	847
Leu Tyr Ala Asn Ile Cys Phe Arg His His Glu Thr Ser Gly Ser Val	
215	225
220	230
CCT ACA GAC TAT CTT CAG CTG ATG GTG TAT GTC GTT AAA ACC AGC ATC	895
Pro Thr Asp Tyr Leu Leu Met Val Tyr Val Val Lys Thr Ser Ile	
235	240
245	
AAA ATC CCA AGT TCT CAT AAC CTG ATG AAA GGA GGG AGC ACG AAA AAC	943
Lys Ile Pro Ser Ser His Asn Leu Met Lys Gly Gly Ser Thr Lys Asn	
250	255
260	265
TGG TCG GGC AAT TCT GAA TTC CAC TTT TAT TAT TCC ATA AAT GTT GGG GGA	991
Trp Ser Gly Asn Ser Glu Phe His Phe Tyr Ser Ile Asn Val Gly Gly	
265	270
275	

FIG.1D

TTT	TTC	AAG	CTC	CGA	GCT	GGT	GAA	GAA	ATT	AGC	ATT	CAG	GTG	TCC	AAC	1039
Phe	Phe	Lys	Leu	Arg	Ala	Gly	Glu	Glu	Ile	Ser	Ile	Gln	Val	Ser	<u>Asn</u>	
280						285					290					
CCT	TCC	CTG	CTG	GAT	CCG	GAT	CAA	GAT	GCG	ACG	TAC	TTT	GGG	GCT	TTC	1087
Pro	Ser	Leu	Leu	Asp	Pro	Asp	Gln	Asp	Ala	Thr	Tyr	Phe	Gly	Ala	Phe	
295					300					305					310	
AAA	GTT	CAG	GAC	ATA	GAC	T	GAGACTCATT	TCGTGGAACA	TTAGCATGGA							1136
Lys	Val	Gln	Asp	Ile	Asp											
					315											
TGTCCTAGAT	GTTTGGAAC	TTCTTAAAAA	ATGGATGATG	TCTATACATG	TGTAAGACTA											1196
CTAAGAGACA	TGGCCCACGG	TGTATGAAAC	TCACAGCCCT	CTCTCTTGAG	CCTGTACAGG											1256
TTGTGTATAT	GTAAGTCCA	TAGGTGATGT	TAGATTTCATG	GTGATTACAC	AACGGTTTTA											1316

FIG.1E

CAATTTTGA	ATGATTTTCCT	AGAATTGAAC	CAGATTGGGA	GAGGTATTCC	GATGCTTATG	1376
AAAAACTTAC	ACGTGAGCTA	TGGAAGGGGG	TCACAGTCTC	TGGGTCTAAC	CCCTGGACAT	1436
GTGCCACTGA	GAACCTTGAA	ATTAAGAGGA	TGCCATGTCA	TTGCAAAGAA	ATGATAGTGT	1496
GAAGGGTTAA	GTTCTTTTGA	ATTGTTACAT	TGCGCTGGGA	CCTGCAAATA	AGTTCCTTTT	1556
TTCTAATGAG	GAGAGAAAAA	TATATGTATT	TTTATATAAT	GTCTAAAGTT	ATAT TTCAGG	1616
TGTAATGTTT	TCTGTGCAAA	GTTTTGTAAA	TTATATT TGT	GCTATAGTAT	TTGATTCAAA	1676
ATATT TAAAA	ATGTCTCACT	GTTGACATAT	TTAATGTTTT	AAATGTACAG	ATGTATT TAA	1736
CTGGTGCACT	TTGTAATTCC	CCTGAAGGTA	CTCGTAGCTA	AGGGGGCAGA	ATACTGTTTC	1796
TGGTGACCAC	ATGTAGTTTA	TTTCTTTATT	CTTTT TAACT	TAATAGAGTC	TTCAGACTTG	1856

FIG.1F

TCAAAACTAT GCAAGCAAAA TAAATAAATA AAAATAAAAT GAATACCTTG AATAATAAGT	1916
AGGATGTTGG TCACCAGGTG CCTTTCAAAT TTAGAAAGCTA ATTGACTTTA GGAGCTGACA	1976
TAGCCAAAAA GGATACATAA TAGGCTACTG AAATCTGTCA GGAGTATTTA TGCAATTATT	2036
GAACAGGTGT CTTTTTTTAC AAGAGCTACA AATTGTAAAT TTTGTTTCTT TTTTTTCCCA	2096
TAGAAAATGT ACTATAGTTT ATCAGCCAAA AAACAATCCA CTTTTTAATT TAGTGAAAGT	2156
TATTTTATTA TACTGTACAA TAAAAGCATT GTCTCTGAAT GTTAATTTTT TGGTACAAAA	2216
AATAAATTG TACGAAAACC TGAAAAAAA AAAAAGGG CGGCCGCTCT	2276
AGAGGGCCCT ATTCTATAG	2295

FIG.1G

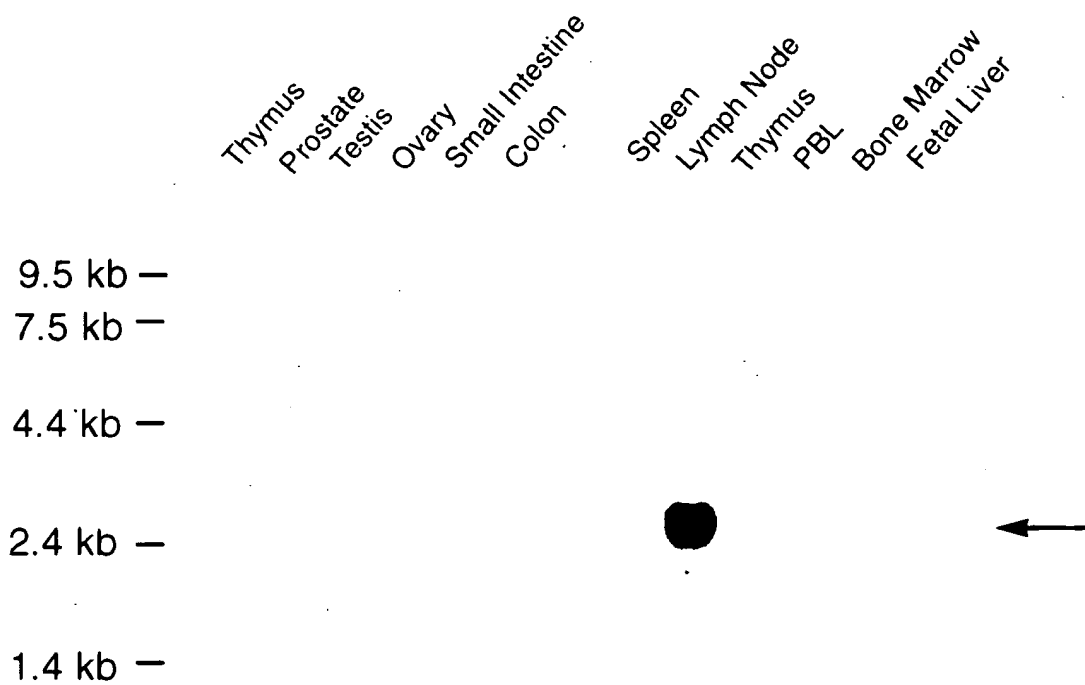


FIG.3



FIG.2A

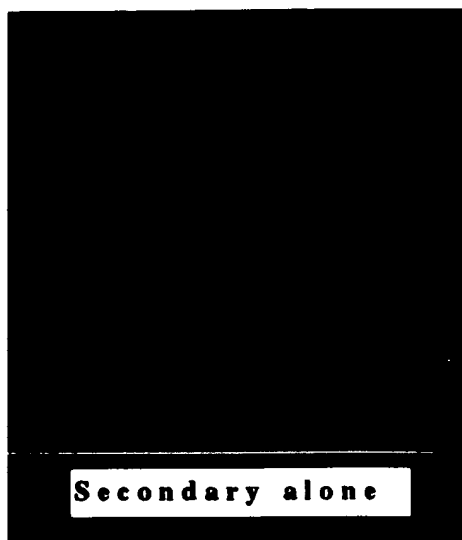


FIG.2B

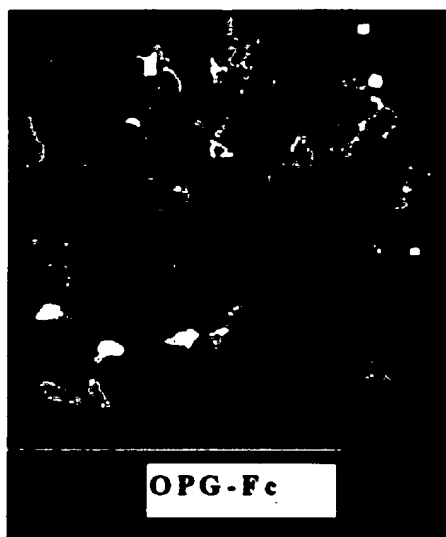
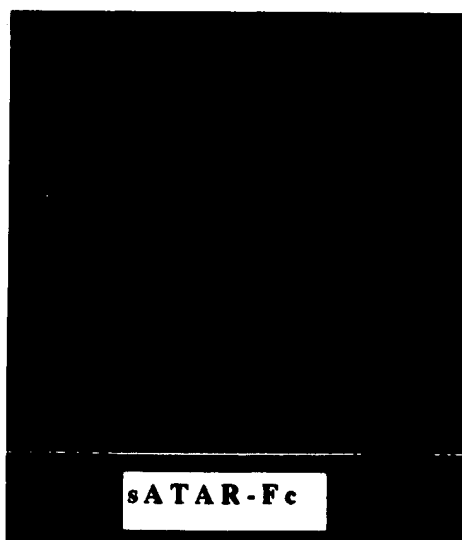


FIG.2C



10 30 50  
AAGCTTGGTACCGAGCTCGGATCCACTACTCGACCCACGGCTCCGGCGGCCCCAGGAGCC

70 90 110  
AAAGCCGGGCTCCAAGTCGGCGCCCCACGTCCGAGGCTCCGCCCGCAGCCTCCGGAGTTGGC

130 150 170  
CGCAGACAAGAAGGGAGGGAGCGGGAGAGGGAGGAGAGCTCCGAAGCAGAGGGCCGAG

190 210 230  
CGCCATGCGCGCGCCAGCAGAGACTACACCAAGTACCTGCGTGGCTCGGAGAGATGGG  
M R R A S R D Y T K Y L R G S E E M G

250 270 290  
CGGCGGCCCCGGAGCCCCGACGAGGGCCCCCTGCACGCCCCCGCCGCTGCGCCGCA  
G G P G A P H E G P L H A P P P A P H

310 330 350  
CCAGCCCCCGCGCTCCCGCTCCATGTTGTCGGCCCTCCTGGGCTGGGCTGGGCCA  
Q P P A A S R S M F V A L L G L G L G Q

370 390 410  
GGTTGTCTGCAGCGTCGCCCTGTCTTCTATTTCAGAGCGCAGATGGATCCTAATAGAT  
V V C S V A L F F Y F R A Q M D P N R I

FIG. 4A

430 450 470  
ATCAGAAGATGGCACTCACTGCATTTATAGAATTTTGAGACTCCATGAATGCAGATTT  
S E D G T H C I Y R I L R L H E N A D F

490 510 530  
TCAAGACACAACCTCTGGAGAGTCAAGATACAAAATTAATACCTGATTCATGTAGGAGAAT  
Q D T T L E S Q D T K L I P D S C R R I

550 570 590  
TAAACAGGCCCTTTCAAGGAGCTGTGCAAAAGGAATTACAACATATCGTTGGATCACAGCA  
K Q A F Q G A V Q K E L Q H I V G S Q H

610 630 650  
CATCAGAGCAGAGAAAGCGATGGTGGATGGCTCATGGTTAGATCTGGCCAAAGAGGAGCAA  
I R A E K A M V D G S W L D L A K R S K

670 690 710  
GCTTGAAGCTCAGCCCTTTGCTCATCTCACTATTAAATGCCACCGACATCCCATCTGGTTC  
L E A Q P F A H L T I N A T D I P S G S

730 750 770  
CCATAAGTGAGTCTGTCTCTTGTGTACCATGATCGGGTGGCCAAAGATCTCCAACAT  
H K V S L S S W Y H D R G W A K I S N M

FIG.4B

790 810 830  
GACTTTTAGCAATGGAAACTAATAGTTAATCAGGATGGCTTTTATTACCTGTATGCCAA  
T F S N G K L I V N Q D G F Y Y L Y A N

850 870 890  
CATTTGCTTTCGACATCATGAACCTTCAGGAGACCTAGCTACAGAGTATCTTCAACTAAT  
I C F R H H E T S G D L A T E Y L Q L M

910 930 950  
GGTGTAAGTCACTAAACCAGCATCAAAATCCCAAGTTCTCTCATACCTGATGAAGGAGG  
V Y V T K T S I K I P S S H T L M K G G

970 990 1010  
AAGCACCAAGTATTGGTCAGGGAATTCTGAATTCCATTTTTATTCATATAACGTTGGTGG  
S T K Y W S G N S E F H F Y S I N V G G

1030 1050 1070  
ATTTTAAAGTTACGGTCTGGAGAGGAAATCAGCATCGAGTCTCCAACCCCTCCTTACT  
F F K L R S G E E I S I E V S N P S L L

1090 1110 1130  
GGATCCGGATCAGGATGCAACATACTTTTGGGGCTTTTAAAGTTCGAGATATAGATTGAGC  
D P D Q D A T Y F G A F K V R D I D

FIG.4C

1150	1170	1190
CCCAGTTTTGGAGTGTATGTATTTCCCTGGATGTTTGGAACATTTTAAACAAGCC		
1210	1230	1250
AAGAAAGATGATATAGGTGTGTGAGACTACTAAGAGGCATGGCCCCAACGGTACACGAC		
1270	1290	1310
TCAGTATCCATGCTCTTGACCTTGTAGAGAAACACGCCGTATTTACAGCCAGTGGGAGATGT		
1330	1350	1370
TAGACTCATGGTGTACACAATGGTTTTTTAAATTTTGTAATGAATTCCTAGAATTAAA		
1390	1410	1430
CCAGATTGGAGCAATTACGGGTGACCTTATGAGAACTGCATGTGGGCTATGGGAGGGG		

FIG.4D

1450 1470 1490  
TGGTCCCTGGTCATGTGCCCCCTTCGCAGCTGAAGTGGAGAGGGTGTCTATCTAGCGCAAT

1510 1530 1550  
TGAAGGATCATCTGAAGGGCAAATTCTTTTGAATTGTTACATCATGCTGGAACCTGGCAA

1570 1590 1610  
AAAATACCTTTTCTAATGAGGAGAGAAAAATATATGTATTTTATATAATCTAAAGTTA

1630 1650 1670  
TATTCAGATGTAATGTTTTCTTTGCAAGTATTGTAAATTATATTTGTGCTATAGTATT

1690 1710 1730  
TGATTCAAAATATTTAAAAATGTCCTTGCTGTGACATATTTAATGTTTTTAAATGTACAGA

1750 1770 1790  
CATATTTAACTGGTGCACTTTGTAAATTCCCTGGGAAACTTGCAGCTAAGGAGGGGAA

1810 1830 1850  
AAAAATGTTGTTCCCTAATATCAAAATGCAGTATATTCTTCGTTCTTTTAAAGTTAATAG

FIG.4E

1870	1890	1910
ATTTTTCAGACTTGTCAAGCCTGTGCAAAAATTAAATGGATGCCTTGAAATAAAG		
1930	1950	1970
CAGGATGTTGGCCACCAGGTGCCCTTTCAAATTTAGAACTAATTGACTTTAGAAAGCTGA		
1990	2010	2030
CATTGCCAAAAGGATACATAATGGGCCACTGAAATCTGTCAAGAGTAGTTATATAATTG		
2050	2070	2090
TTGAACAGGTGTTTTTCCACAAGTGCCGCAAAATTGTACCTTTTTTTTTTCAAAATAG		
2110	2130	2150
AAAAGTTATTAGTGTTTATCAGCAAAAAGTCCAAATTTTAATTAGTAAATGTTATCTT		
2170	2190	2210
ATACTGTACAATAAAACATTGCCCTTTGAAATGTTAATTTTGGTACAAAAATAATTTA		
2230	2250	2270
TATGAAAAAAAAGGGCGCGCTCTAGAGGGCCCTATTCTATAG		

FIG.4F

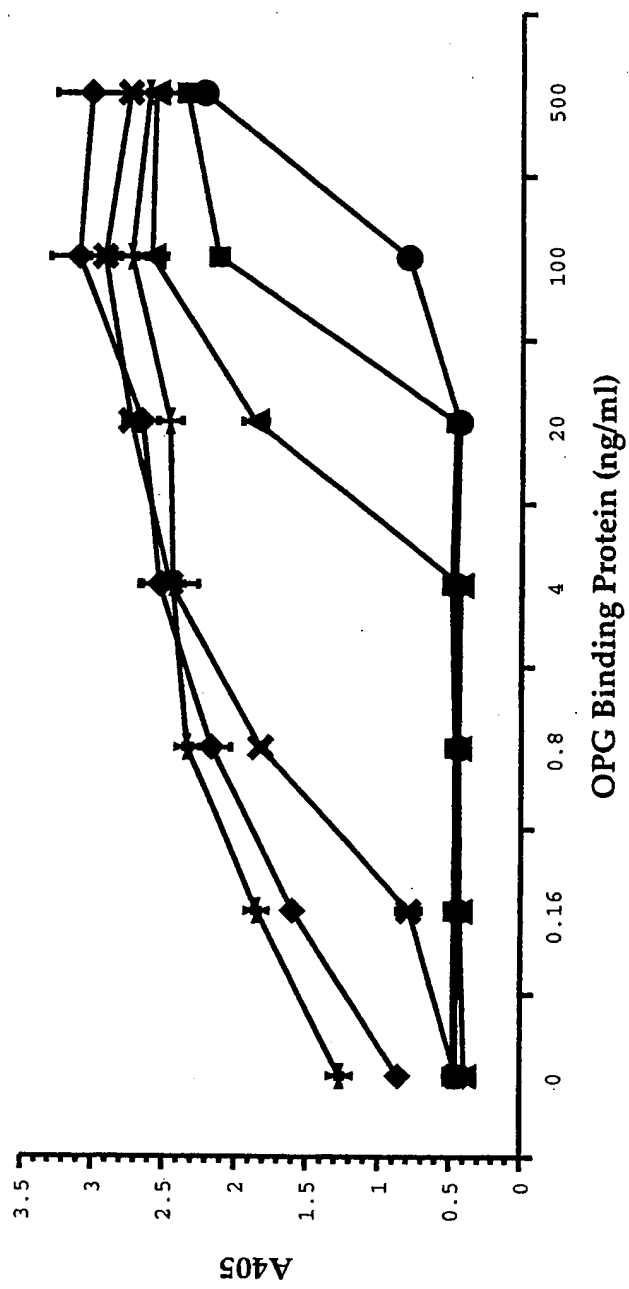


FIG. 5



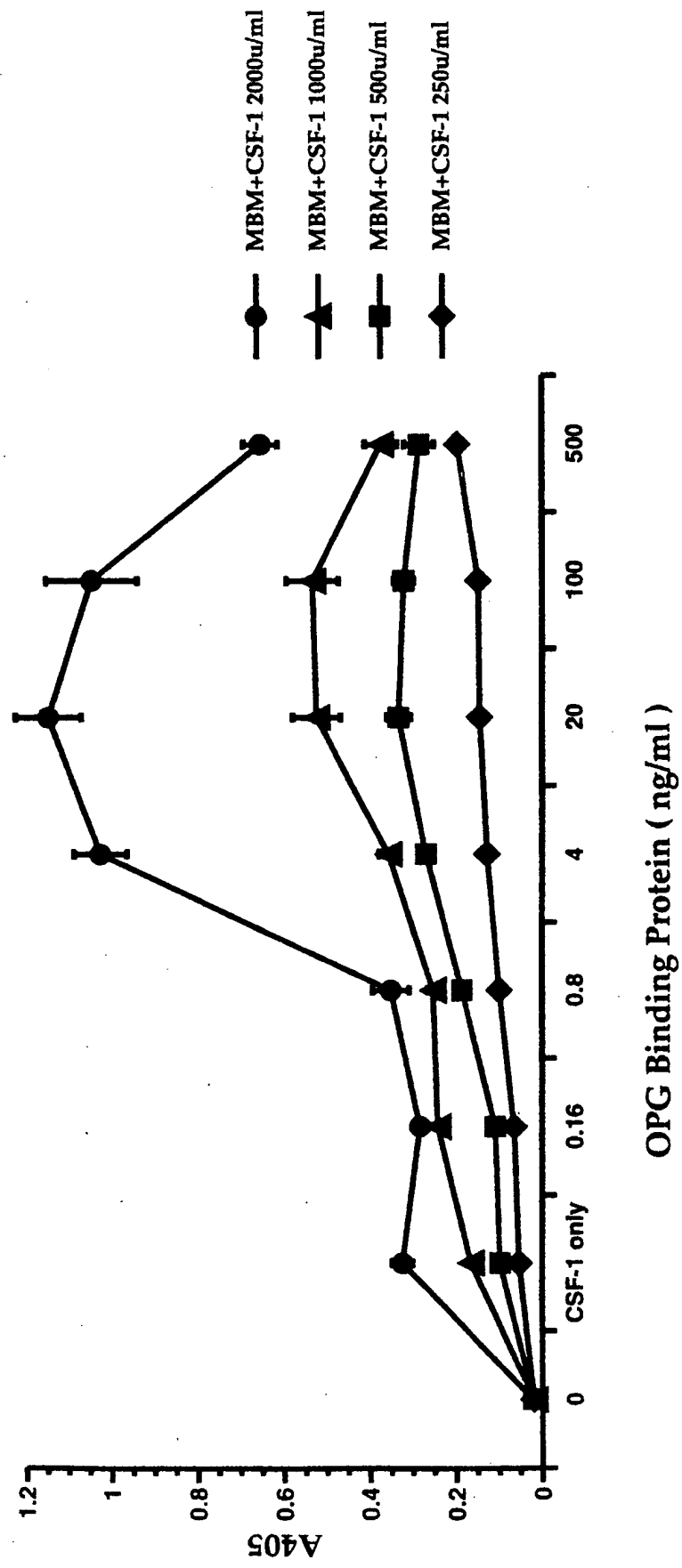


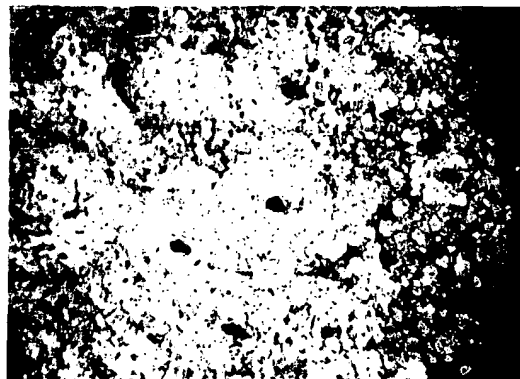
FIG. 6

**FIG.7A**

**Toluidine Blue Staining**



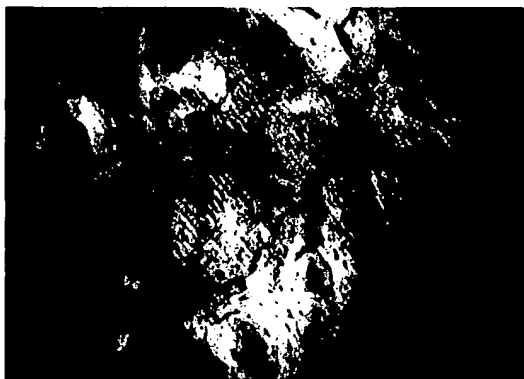
**TRAP staining**



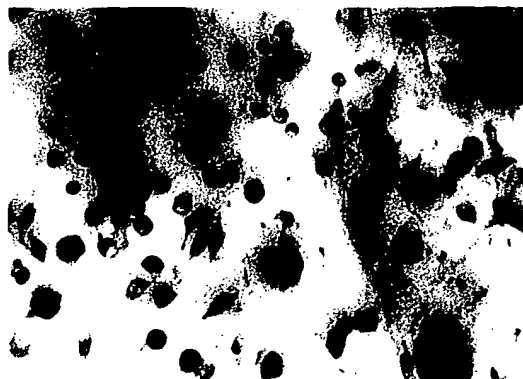
**Bone Marrow Cells + M-CSF-1**

**FIG.7B**

**Toluidine Blue Staining**



**TRAP staining**



**Bone Marrow Cells + OPG Binding Protein**

**FIG.7C**

**Toluidine Blue Staining**



**TRAP staining**



**Bone Marrow Cells + M-CSF-1 + OPG Binding Protein**

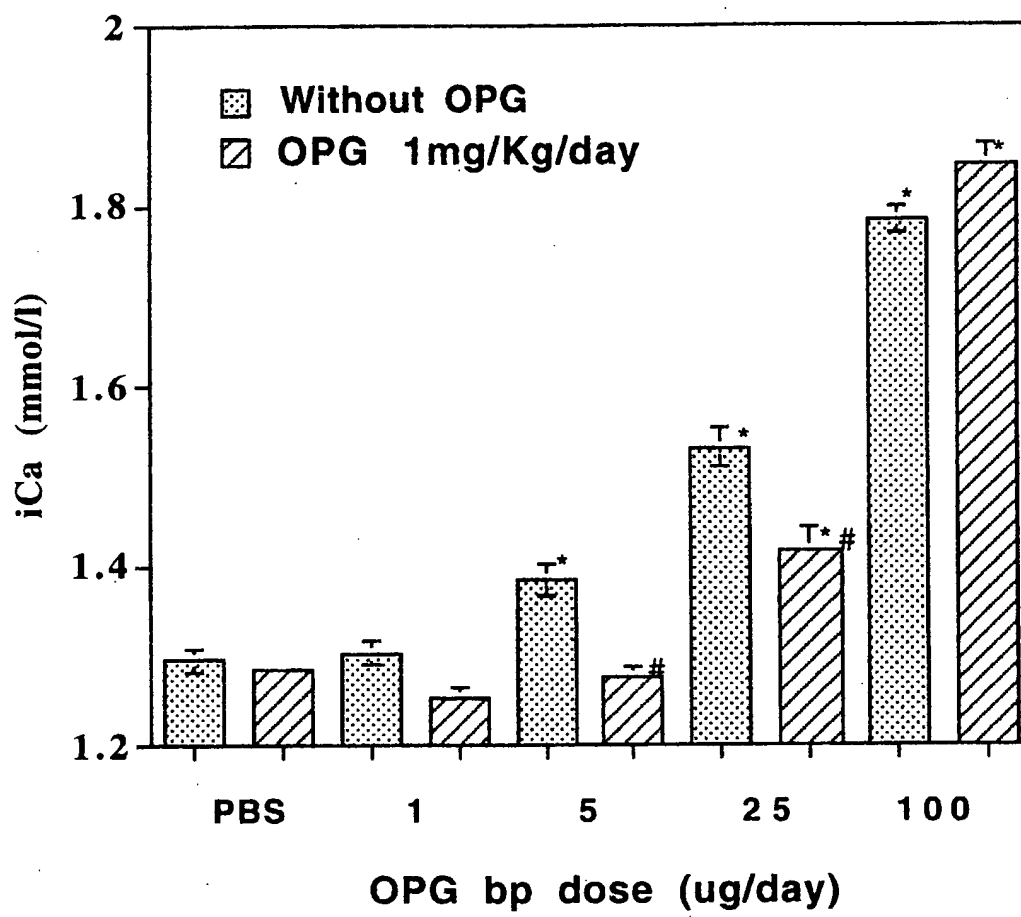


FIG. 8

**PBS**



**FIG. 9A**

**OPGbp 5ug/d**



**FIG. 9B**

**OPGbp 25ug/d**



**FIG. 9C**

**OPGbp100ug/d**



**FIG. 9D**

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☒ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☐ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**